PRELIMINARY AMENDMENT

In the Claims:

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1. (Original) An immunogenic fusion protein comprising (a) a modified NS3 polypeptide comprising at least one amino acid substitution to the HCV NS3 region, such that protease activity is inhibited, and (b) at least one polypeptide derived from a region of the HCV polyprotein other than the NS3 region.

2. (Original) The fusion protein of claim 1, wherein the modification comprises a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein.

3. (Original) The fusion protein of claim 1, wherein the protein comprises a modified NS3 polypeptide, an NS4 polypeptide, an NS5a polypeptide, and optionally a core polypeptide.

4. (Original) The fusion protein of claim 3, wherein the protein further comprises an NS5b polypeptide, and optionally a core polypeptide.

5. (Original) The fusion protein of claim 3, wherein the protein further comprises an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, and optionally a core polypeptide.

6. (Original) The fusion protein of claim 3, wherein the protein further comprises an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, and optionally a core polypeptide.

7. (Original) The fusion protein of claim 3, wherein the protein further comprises an E2 polypeptide, and optionally a core polypeptide.

8. (Original) The fusion protein of claim 3, wherein the protein further comprises an E1 polypeptide, an E2 polypeptide, and optionally a core polypeptide.

9. (Original) The fusion protein of claim 1, wherein the protein comprises an E2 polypeptide, a modified NS3 polypeptide, and optionally a core polypeptide.

10. (Original) The fusion protein of claim 1, wherein the protein comprises an E1 polypeptide, an E2 polypeptide, a modified NS3 polypeptide, and optionally a core polypeptide.

11. (Original) The fusion protein of claim 1, wherein the polypeptides of (a) and (b) are derived from the same HCV isolate.

12. (Original) The fusion protein of claim 1, wherein at least one of the polypeptides present in the fusion is derived from a different isolate that the modified NS3 polypeptide.

13. (Original) An immunogenic fusion protein consisting essentially of, in amino terminal to carboxy terminal direction:

(a) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, and an NS5a polypeptide;

(b) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and an NS5b polypeptide;

(c) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-

1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, and an NS5a polypeptide;

(d) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, and an NS5a polypeptide;

(e) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and an NS5b polypeptide;

(f) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and an NS5b polypeptide;

(g) an E2 polypeptide and a modified NS3 polypeptide comprising substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited;

(h) an E1 polypeptide, an E2 polypeptide and a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited;

(i) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide and a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited; or

(j) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide and a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited.

14. (Original) An immunogenic fusion protein consisting essentially of, in amino terminal to carboxy terminal direction:

(a) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, and a core polypeptide;

(b) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, an NS5b polypeptide and a core polypeptide;

(c) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and a core polypeptide;

(d) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and a core polypeptide;

(e) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, an NS5b polypeptide and a core polypeptide;

(f) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, an NS5b polypeptide and a core polypeptide;

(g) an E2 polypeptide, a modified NS3 polypeptide comprising substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide;

(h) an E1 polypeptide, an E2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide;

(i) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide; or

(j) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide.

15. (Original) A modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited when the modified NS3 polypeptide is present in an HCV fusion protein.

16. (Original) A composition comprising an immunogenic fusion protein according to claim 1 in combination with a pharmaceutically acceptable excipient.

17. (Original) A composition comprising an immunogenic fusion protein according to claim 13 in combination with a pharmaceutically acceptable excipient.

18. (Original) A composition comprising an immunogenic fusion protein according to claim 14 in combination with a pharmaceutically acceptable excipient.

19. (Original) A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 16.

20. (Original) A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 17.

21. (Original) A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 18.

22. (Original) A method for producing a composition comprising combining the immunogenic fusion protein of claim 1 with a pharmaceutically acceptable excipient.

23. (Original) A method for producing a composition comprising combining the immunogenic fusion protein of claim 13 with a pharmaceutically acceptable excipient.

24. (Original) A method for producing a composition comprising combining the immunogenic fusion protein of claim 14 with a pharmaceutically acceptable excipient.

25. (Original) A polynucleotide comprising a coding sequence encoding a fusion protein according to claim 1.

26. (Original) A polynucleotide comprising a coding sequence encoding a fusion protein according to claim 13.

27. (Original) A polynucleotide comprising a coding sequence encoding a fusion protein according to claim 14.

28. (Original) A polynucleotide comprising a coding sequence encoding a polypeptide according to claim 15.

29. (Original) A recombinant vector comprising:

(a) the polynucleotide of claim 25; and

(b) at least one control element operably linked to said polynucleotide, whereby said coding sequence can be transcribed and translated in a host cell.

30. (Original) A recombinant vector comprising:

(a) the polynucleotide of claim 26; and

(b) at least one control element operably linked to said polynucleotide, whereby said coding sequence can be transcribed and translated in a host cell.

31. (Original) A recombinant vector comprising:

(a) the polynucleotide of claim 27; and

(b) at least one control element operably linked to said polynucleotide, whereby said coding sequence can be transcribed and translated in a host cell.

32. (Original) A recombinant vector comprising:

(a) the polynucleotide of claim 28; and

(b) at least one control element operably linked to said polynucleotide, whereby said coding sequence can be transcribed and translated in a host cell.

33. (Original) A host cell comprising the recombinant vector of claim 29.

34. (Original) A host cell comprising the recombinant vector of claim 30.

35. (Original) A host cell comprising the recombinant vector of claim 31.

36. (Original) A host cell comprising the recombinant vector of claim 32.

37. (Original) A method for producing an immunogenic fusion protein, said method comprising culturing a population of host cells according to claim 33 under conditions for producing said protein.

38. (Original) A method for producing an immunogenic fusion protein, said method comprising culturing a population of host cells according to claim 34 under conditions for producing said protein.

39. (Original) A method for producing an immunogenic fusion protein, said method comprising culturing a population of host cells according to claim 35 under conditions for producing said protein.

40. (Original) A method for producing a polypeptide, said method comprising culturing a population of host cells according to claim 36 under conditions for producing said polypeptide.

41. (New) An immunogenic fusion protein comprising (a) a modified NS3 domain comprising a substitution of an amino acid corresponding to Ser-1165, numbered relative to the full-length HCV-1 polyprotein, such that protease activity is inhibited; (b) an NS4 domain; (c) an NS5a domain; (d) an NS5b domain; and (e) optionally a core polypeptide comprising the sequence of amino acids depicted at amino acid positions 1772-1892 of SEQ ID NO:6.

42. (New) The immunogenic fusion protein of claim 41, wherein said protein comprises a core polypeptide consisting of the sequence of amino acids depicted at amino acid positions 1772-1892 of SEQ ID NO:6.

43. (New) An immunogenic fusion protein comprising (a) a truncated E2 polypeptide consisting of an amino acid sequence corresponding to amino acids 384-715, numbered relative to the full-length HCV-1 polyprotein; (b) a modified NS3 domain comprising a substitution of an amino acid corresponding to Ser-1165, numbered relative to the full-length HCV-1 polyprotein, such that protease activity is inhibited; (b) an NS4 domain; (c) an NS5a domain; (d) an NS5b domain; and (e) optionally a core polypeptide comprising the sequence of amino acids depicted at amino acid positions 1772-1892 of SEQ ID NO:6.

44. (New) The immunogenic fusion protein of claim 43, wherein said protein comprises a core polypeptide consisting of the sequence of amino acids depicted at amino acid positions 1772-1892 of SEQ ID NO:6.

45. (New) A composition comprising an immunogenic fusion protein according to claim 41 in combination with a pharmaceutically acceptable excipient.

46. (New) A composition comprising an immunogenic fusion protein according to claim 43 in combination with a pharmaceutically acceptable excipient.

47. (New) A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 45.

48. (New) A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 46.

49. (New) A method for producing a composition comprising combining the immunogenic fusion protein of claim 41 with a pharmaceutically acceptable excipient.

50. (New) A method for producing a composition comprising combining the immunogenic fusion protein of claim 43 with a pharmaceutically acceptable excipient.

51. (New) A polynucleotide comprising a coding sequence encoding a fusion protein according to claim 41.

52. (New) A polynucleotide comprising a coding sequence encoding a fusion protein according to claim 43.

53. (New) A recombinant vector comprising:

(a) the polynucleotide of claim 51; and

(b) at least one control element operably linked to said polynucleotide, whereby said coding sequence can be transcribed and translated in a host cell.

54. (New) A recombinant vector comprising:

(a) the polynucleotide of claim 52; and

(b) at least one control element operably linked to said polynucleotide, whereby said coding sequence can be transcribed and translated in a host cell.

55. (New) A host cell comprising the recombinant vector of claim 53.

56. (New) A host cell comprising the recombinant vector of claim 54.

57. (New) A method for producing an immunogenic fusion protein, said method comprising culturing a population of host cells according to claim 55 under conditions for producing said protein.

58. (New) A method for producing an immunogenic fusion protein, said method comprising culturing a population of host cells according to claim 56 under conditions for producing said protein.